

WO 00/38627

**PREPARATIONS COMPRISING ALPHA-POLYGLUCANS
FOR TOPICAL APPLICATION**


Description

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The present invention relates to a cosmetic or medicinal preparation for topical application, comprising at least one biotechnologically obtained water-insoluble linear poly- α -glucan, in particular a skincare composition.

- 10 The use of starch-based polysaccharides such as polyglucans for cosmetic purposes has been known since time immemorial.

- 15 Recently, polysaccharide products for cosmetic and therapeutic purposes which have specific profiles of properties have increasingly been developed. For example, H. Eggensperger, M. Wilker in SÖFW Journal, 123rd Volume 8/97, pages 542 to 546, "Multiaktivwirksame Polysaccharide, Teil I – Pilzextrakte [Multiactive Polysaccharides, Part I – Fungus extracts] describes for beta-polyglucans from fungi such as yeasts and carboxymethylated derivatives thereof a high care action for irritated, dry skin.

- 20 Particularly advantageous effects on the skin have been demonstrated for beta-1,3-polyglucans with beta-1,6 linkages, for which, in addition, an immunostimulating action and tumor activity have been observed (loc. cit. F. Züllli et al., loc. cit. pages 535 to 541).

- 25 Cyclodextrins, cyclic alpha-, beta- or gamma-1,4-oligosaccharides with 6 to 8 glucan units are also being used increasingly for functional skin care since they form inclusion compounds with a large number of active ingredients and care substances and as a result can effect delayed release of these substances at the site of application (U. Citemesi, M. Scalacchitano in Cosmetics and Toiletries magazine, Volume 110, March 1995, pages 53 to 61 "Cyclodextrins in functional dermocosmetics"). Furthermore, it is proposed to use glycogen obtained biotechnologically or obtained from marine molluscs, a highly branched poly-1,4- α -glucan with branches in the 6-position, for cosmetic purposes (M. Pauly, G. Pauly "New Polysaccharides Interest in Care Cosmetology" IN-COSMETICS 1997, Conference Proceedings, pages 417-444, Verlag für chemische Industrie, H.Ziolkowsky GmbH, 1998).
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Examples of decorative cosmetics are creams, powders or bases for make-up, e.g. blusher, eye shadow, lipsticks.

For the purposes of the invention, "biotechnological preparation" means the use of biocatalytic, including biotransformatory, or fermentation processes.

Water-insoluble linear poly- α -glucans prepared by biocatalysis (also: biotransformation) for the purposes of this invention means that the linear polyglucan is prepared by catalytic reaction of monomeric basic building blocks such as oligomeric saccharides, e.g. of monosaccharides and/or disaccharides, by using a "biocatalyst", usually an enzyme, under suitable conditions. In this connection, the expression "in vitro biocatalysis" is also used.

Within the language usage of the invention, water-insoluble linear polyglucans from fermentations are linear polyglucans which are obtained by fermentation processes using naturally occurring organisms, such as fungi, algae, bacilli, bacteria or protists or using non-naturally occurring organisms, but using natural organisms modified using genetic methods of the general definition, such as fungi, algae, bacilli, bacteria or protists, or which can be obtained with the use and assistance of fermentation processes. In this connection, the expression used is also "in vivo biocatalysis".

Examples of such microorganisms are *Pichia pastoris*, *Trichoderma reesei*, *Staphylococcus carnosus*, *Escherichia coli* or *Aspergillus niger*.

Advantageous processes for the biotechnological production are described, for example, in WO 95/31553 or the previously unpublished German patent application from the Applicant with the official file reference 198 27 978.5.

According to the processes described therein, a sucrose solution is treated with amylosucrase, poly-1,4- α -D-glucan and fructose being formed directly with cleavage of the sugar bond.

Further suitable enzymes are polysaccharide synthases, starch synthases, glycol transferases, 1,4- α -D-glucan transferases, glycogen synthases and also phosphorylases.

In contrast to poly- α -glucans which are isolated from natural sources, such as plants, the linear water-insoluble polyglucans obtained here have a particularly homogeneous profile of properties, e.g. with regard to the molecular weight distribution, they contain no, or at worst only very small amounts of, undesired byproducts which have to be separated off at great

expense or could trigger allergic reactions, and can be easily reproduced in an exactly specified manner.

Thus, poly- α -glucans with varying properties such as molecular weights etc. can be obtained as required in a defined and readily reproducible manner.

Although it is also possible to obtain comparatively homogeneous products using chemical or enzymatic debranching, in many cases a remainder of undebranched or only inadequately debranched starting material is left behind, which can only be separated off with difficulty.

Water-insoluble linear poly- α -glucans for the purposes of the present invention are polysaccharides built up from glucans as monomeric building blocks such that the individual building blocks are always linked together in the same manner. Each basic unit or building block defined in this way has exactly two linkages, in each case one to one other monomer. The only exceptions to this are the two basic units which form the start and the end of the polysaccharide. These have only one linkage to one further monomer and form the end-groups of the linear polyglucan.

If the basic unit has three or more linkages, this is referred to as branching. In this context, the number of hydroxyl groups per 100 basic units which are not involved in constructing the linear polymer backbone and form the branches gives the "degree of branching".

According to the invention, the linear water-insoluble poly- α -glucans have a degree of branching of at most 8%, i.e. they have at most 8 branches per 100 basic units. The degree of branching is preferably less than 4% and in particular at most 2.5%.

Particular preference is given to poly- α -glucans whose degree of branching in the 6-position is less than 4%, preferably at most 2% and in particular at most 0.5%, and in the other positions, e.g. in the 2- or 3-position, preferably in each case at most 2% and in particular 1%.

Particular preference is also given to poly- α -glucans whose degree of branching in the 6-position is less than 0.5%.

Of particular suitability for the invention are poly- α -glucans which do not have branches or whose degree of branching is so minimal that it is no longer detectable by traditional methods.

Examples of preferred water-insoluble linear poly- α -glucans are linear poly- α -D-glucans, the nature of the linkage being unimportant, provided there is linearity within the meaning of the invention. A particularly preferred example is poly-1,4- α -D-glucan.

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For the present invention, the prefixes "alpha" or "D" refer solely to the linkages which form the polymer backbone and not to the branches.

10 Biotechnological and, in particular, biocatalytic methods have the advantage that the degree of branching can be set in a controllable manner and, in particular, water-insoluble linear poly- α -glucans can be obtained directly, such as, for example, the preferred poly-1,4- α -D-glucans which do not contain branches, or whose degree of branching is below the detection limit for conventional analytical methods.

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For the present invention, the term "water-insoluble poly- α -glucan" is understood as meaning compounds which, according to the definition in the German Pharmacopeia (DAB = Deutsches Arzneimittelbuch, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, Govi-Verlag, Frankfurt [lacuna] edition, 1987), fall into the categories "slightly soluble", "sparingly soluble", "very sparingly soluble" and "virtually insoluble" compounds, corresponding to classes 4 to 7.

25 In the case of the polyglucans used according to the invention, this means that at least 98% of the amount used, in particular at least 99.5%, are insoluble in water under standard conditions ($T = 25^{\circ}\text{C}/-20\%$, $p = 101325$ Pascal $\pm 20\%$) (corresponding to classes 4 and 5, respectively).

30 For the present invention, preference is given to sparingly soluble to virtually insoluble compounds, in particular very sparingly soluble to virtually insoluble compounds.

"Very sparingly soluble" corresponding to class 6 can be illustrated by the following protocol:

35 One gram of the polyglucan to be investigated is heated in 1 l of deionized water to 130°C at a pressure of 1 bar. The resulting solution only remains stable briefly for a few minutes. Upon cooling under standard conditions, the substance precipitates out again. After cooling to room temperature

and separation by means of centrifugation, at least 66% of the amount used can be recovered, taking into consideration experimental losses.

For the present invention the biotechnologically obtained poly- α -glucan can
5 be used as it is. If desired, it can be subjected to an additional treatment.

Thus, the water-insoluble linear poly- α -glucans can be modified, for example, by chemically modifying the poly- α -glucans by esterification and/or etherification in one or more positions which are not involved in the linear
10 linkage. In the case of the preferred 1,4-linked poly- α -glucans, the modification can take place in the 2-, 3- and/or 6-position.

For the purposes of the invention, modification means that the hydroxyl groups present which are not involved in the linkage are chemically
15 changed. This excludes ring opening of the glucan units, as occurs, for example, during oxidative carboxylation or hydrolysis. Measures for such modifications are sufficiently known to the person skilled in the art.

The poly- α -glucans can be used in the form of "alpha-amylase-resistant" poly- α -glucans, as are described using the example of poly(1,4- α -D-glucan) in the previously unpublished German patent application with the
20 official file reference 198 30 618.0 from the Applicant.

Alpha-amylase-resistant poly- α -glucans can be obtained by preparing a suspension or dispersion of water-insoluble polyglucans and water, heating
25 the suspension or dispersion to a temperature in the range from 50 to 100°C, allowing the resulting paste-like mixture to cool to a temperature in the range from 50°C down to the freezing point, preferably 35 to 15°C, 27 to 22°C, 16 to 0°C or 6 to 2°C, over a period of from 1 to 72 h, preferably 1
30 to 36 h and in particular 15 to 30 h, and retrograding the paste-like mixture at a temperature which is lower than the temperature of the heated paste-like mixture in a temperature range from 90 to 4°C, and, if desired, drying or dewatering the resulting product.

35 The poly- α -glucan can also be used as thermoplastic polyglucan obtainable by melting linear water-insoluble polyglucan and adding at least 20% by weight, preferably at least 30% by weight, of a softener such as sorbitol, glycerol, condensation products and oligomers thereof, DMSO,

succinic acid, citric acid monohydrate, malic acid, tartaric acid, etc. at about 170°C.

A description of suitable measures and properties of thermoplastic polyglucans using the example of the preferred linear water-insoluble poly-1,4- α -D-glucan is given in the previously unpublished German patent application with the official file reference 198 52 826, to which express reference is made here.

To improve the incorporability, the thermoplastic poly- α -glucan can be granulated beforehand.

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The molecular weights M_w (weight-average, determined by means of gel permeation chromatography relative to calibration with a pullulan standard) of the water-insoluble linear poly- α -glucans used according to the invention can vary within a wide range from 0.75×10^2 to 10^7 g/mol. The molecular

15 weight M_w is preferably in a range from 10^3 g/mol to 10^6 g/mol and particularly preferably from 10^3 g/mol to 10^5 g/mol. A further advantageous range is from 2×10^3 to 8×10^3 . Corresponding ranges apply for the preferably used poly-1,4- α -D-glucan.

The molecular weight distribution or polydispersity M_w/M_n can likewise vary within wide ranges depending on the polyglucan preparation process. Preferred values are from 1.01 to 50, in particular from 1.01 to 15, no values being particularly preferred, e.g. from 1.01 to 2.5.

For the preparation of the topical preparation, it is possible to use a single water-insoluble linear poly- α -glucan or a mixture of two or more thereof.

It is also possible to use mixtures of biotechnologically obtained, water-insoluble linear poly- α -glucan and polyglucans from other sources.

Due to their nature-identity, excellent biocompatibility can be expected for the water-insoluble linear poly- α -glucans used according to the invention.

Depending on the desired use, the topical preparations according to the invention can comprise suitable further ingredients customary for the respective purpose.

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Examples of such ingredients as can be used, in particular, also for cosmetic compositions are emulsifiers, oils, waxes, fats or other customary constituents of a cosmetic formulation, such as alcohols, polyols, polymers, foam stabilizers, electrolytes, oils, volatile hydrocarbons, silicone

derivatives or silicone derivatives, active ingredients, humectants, fillers, color pigments, luster pigments, dyes, UV filters, perfume oils, antioxidants, stabilizers, antiinflammatory additives, circulation-stimulating additives, preservatives, bactericides, deodorizing substances, antiperspirants, insect
5 repellants, vitamins, proteins, antifoams, thickeners, emollients, moisturizers and/or humectants, etc.

A list of possible approved ingredients for cosmetic compositions, as can, in principle, also be used for the present invention, is given in the brochure
10 "Kosmetika – Inhaltsstoffe – Funktionen" [Cosmetics – Ingredients – Functions], which has been published by the Industrieverband Körperpflege- und Waschmittel e.V. und dem Fachverband der chemischen Industrie Österreichs, Berufsgruppe Körperpflegemittel, Frankfurt am Main/
Vienna, June 1998.

15 Medicinal topical preparations generally comprise one or more medicaments in effective concentration.

To differentiate between cosmetic and medicinal use and the corresponding products, reference is made to the prevailing provisions in
20 Germany as are laid down, for example, in the Cosmetics Directive or the Foods and Drugs Act.

It goes without saying that the medicinal preparations may comprise the same ingredients as have been mentioned above by way of example for
25 the cosmetic application, provided they are permitted for medicinal purposes.

In general, the ingredients in question are added to the preparations according to the invention in proportions customary for the respective use
30 purpose.

The linear poly- α -glucans used according to the invention can also be particularly highly effective as matrix material for ingredients to be added to the preparations. For example, cosmetic and/or medicinal active
35 ingredients can be present in adsorbed and/or absorbed form on the poly- α -glucans.

Particularly suitable matrix or carrier material are linear poly- α -glucans with a helical tertiary structure, as is formed, for example, by the preferred poly-1,4- α -D-glucan.

5 In this case, the additives, such as active ingredient etc., may be present as an inclusion in the helix, analogously, for example, to the inclusion compounds formed by the cyclodextrins.

10 The preparations according to the invention can be prepared according to the customary rules familiar to the person skilled in the art.

15 The preparations according to the invention can be present in any formulation suitable for the respective use purpose, e.g. as emulsions, such as O/W emulsions, W/O emulsions, multiple emulsions e.g. W/O/W, O/W/O, O/W/O/W, W/O/W/O emulsions etc., the wax-based, anhydrous, hydrodispersions, gels, oils, anhydrous ointments or ointment bases etc.

20 The water-insoluble linear-poly- α -glucans used according to the invention can, in principle, adopt the functions of the customarily used polyglucans from e.g. native sources such as starch in topical preparations.

25 Compared with base materials from native sources, they have the advantage that they can be obtained in a simple manner with high homogeneity and purity.

30 They can thus be used as filler, thickener, binder or gelling agent.

35 In contrast to many pigments, such as, for example, nonmicronized titanium dioxide, the poly- α -glucans used according to the invention do not whiten on the skin, i.e. they look transparent and can therefore advantageously replace such pigments.

Thus, they can be accepted as replacement for substances such as talc or kaolin which, because of their irregular or disk-shaped structure, leads to a harsh feel upon application, e.g. in pigmented products, or can be used as compacting auxiliaries in pressed powders.

In addition, an absorbing effect has been observed for the poly- α -glucans used according to the invention.

Because of this absorbing effect, they are also particularly readily suitable as additive in deodorants, body powders such as body talc, for absorbing excess skin sebum e.g. in anti-oil or antiacne products.

- 5 In addition, it has been possible to observe that they are able to reduce skin roughnesses, overall have a calming effect on the skin, and exert a softening and moisturizing action.

Suitable proportions of poly- α -glucan used according to the invention for creams, lotions, make-up, compact creams and the like are in the range
10 from about 0.5% by weight to about 40% by weight, preferably about 2 to about 10% by weight, for powders from about 0.5 to about 80% by weight, for ointments and pharmaceutical ointments, corresponding proportions can be chosen, the proportions in each case being based on the total weight of the preparation in question.

- 15 It goes without saying that, if required, e.g. for particular applications, it is also possible to use more, e.g. up to 100% by weight, or less poly- α -glucan.

- 20 The proportion of poly- α -glucan in the respective preparations is of course governed by the desired effect and/or the particular formulation of the preparation.

The invention is illustrated below by reference to individual examples.

- 25 For Examples 1 to 4, the poly- α -glucan obtained according to Example 5 was used.

Examples 1 and 2 and Comparative Examples 1 and 2

- 30 Preparation procedure for lotion and cream
The composition for the lotion (Examples 1a, 1b and Comparative Example 1) and the cream (Examples 2a, 2b and Comparative Example 2) are given in Table 1.

- 35 Preliminary preparation:

Fatty phase:

Heat emulsifiers and oils to 70°C with stirring. Add preservatives, here parabens, and dissolve with stirring.

Water phase:

- 5 Heat demin. water to 70°C, dissolve remaining constituents with stirring. Disperse poly- α -glucan.

Preservative solution:

Dissolve preservative (imidazolidinylurea) in demin. water.

10

Preparation:

Initially introduce fatty phase, $t = 68-70^{\circ}\text{C}$. Add water phase ($t = 68-70^{\circ}\text{C}$) with stirring and homogenize. After the addition, stir and homogenize for 20 min, $t = 65-68^{\circ}\text{C}$.

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Cooling:

to 40°C with stirring.

Add preservative solution and perfume oil and stir and homogenize for 5 min.

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Cool to 30°C with stirring.

The creams and lotions according to the invention felt very pleasant upon application and produced a silky feel on the skin.

The addition of water-insoluble linear poly- α -glucan did not lead to whitening on the skin.

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Examples 3a and b and Comparative Example 3

Preparation procedure for compact cream make-up

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The composition is given in Table 2.

Preliminary preparation:

Heat lanolin and oils to 80-82°C. Dissolve antioxidant and film former with stirring. Add premelted waxes ($t = 80^{\circ}\text{C}$).

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Preparation:

Add premix of color pigments, titanium dioxide, talc, mica and poly- α -glucan with stirring and homogenization.

Then stir and homogenize for 30 min, $t = 82^{\circ}\text{C}$.

Emptying:

Empty the bulk air-free into suitable containers.

- 5 Compared with the basic formulation, the preparation according to the invention exhibited a reduced wax-like nature.

Examples 4a and b and Comparative Example 4

- 10 Preparation procedure for foundation

The composition is shown in Table 3.

Preliminary preparation:

Heat emulsifier, consistency regulator and oil to 70°C and mix. Add preservative and dissolve with stirring.

15

Heat demin. water and propylene glycol to 70°C, dissolve active ingredient and stabilizer with stirring. Aspirate premix of color pigments, titanium dioxide and poly- α -glucan with homogenizer operating. Then stir and homogenize for 30 min.

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Preparation:

Aspirate filtered fatty phase ($t = 70^{\circ}\text{C}$) with stirring and homogenization and stir and homogenize for a further 10 min, $t = 65^{\circ}\text{C}$.

25

Cooling:

to 40°C with stirring. Add presolution of preservative in demin. water and perfume oil at 40°C. Then stir and homogenize for 10 min.

Cool to 30°C with stirring and homogenization.

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Compared with the base according to the comparative example, the base according to the invention felt considerably more creamy. In addition, an increase in viscosity was observed.

Table 1

| Component | Comparison 1 | 1a | 1b | Com- parison 2 | 2a | 2b |
|-------------------------------|-----------------|--------|--------|-------------------|--------|--------|
| Sorbitan stearate | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 |
| Polysorbate 60 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| Cetyl alcohol | | | | 2.50 | 2.50 | 2.50 |
| Mineral oil | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 |
| Decyl oleate | 4.00 | 4.00 | 4.00 | 4.00 | 4.00 | 4.00 |
| Glyceryl stearate | 4.00 | 4.00 | 4.00 | 5.00 | 5.00 | 5.00 |
| Dimethicone | 0.50 | 0.50 | 0.50 | 0.20 | 0.20 | 0.20 |
| Parabens | 0.35 | 0.35 | 0.35 | 0.35 | 0.35 | 0.35 |
| | | | | | | |
| | | | | | | |
| Demineralized water (aqua) | 63.30 | 63.30 | 63.30 | 58.60 | 58.60 | 58.60 |
| Allantoin | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 | 0.20 |
| Propylene glycol | 3.50 | 3.50 | 3.50 | 5.00 | 5.00 | 5.00 |
| | | | | | | |
| | | | | | | |
| Demineralized water (aqua) | 10.00 | 8.00 | 5.00 | 10.00 | 8.00 | 5.00 |
| Poly- α -glucan* | | 2.00 | 5.00 | | 2.00 | 5.00 |
| Demineralized water (aqua) | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| Imidazolidinylurea | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| | | | | | | |
| | | | | | | |
| Perfume (fragrance) | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| | | | | | | |
| | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 |

* no INCI name

000000-11595860

Table 2

| Component (INCI) | Comparison 3 | 3a | 3b |
|--------------------------|-----------------|--------|--------|
| Lanolin | 10.10 | 10.10 | 10.10 |
| Mineral oil | 7.85 | 7.85 | 7.85 |
| Castor oil | 2.80 | 2.80 | 2.80 |
| Octyldodecanol | 22.00 | 20.00 | 17.00 |
| Isopropyl palmitate | 5.00 | 5.00 | 5.00 |
| Antioxidant | 0.05 | 0.05 | 0.05 |
| PVP/eicosane copolymer | 0.15 | 0.15 | 0.15 |
| Iron oxide | 0.68 | 0.68 | 0.68 |
| Titanium dioxide * | 2.75 | 2.75 | 2.75 |
| Talc * | 16.07 | 16.07 | 16.07 |
| Mica | 13.90 | 13.90 | 13.90 |
| Poly- α -glucan * | | 2.00 | 5.00 |
| Cera microcritallina | 9.70 | 9.70 | 9.70 |
| Petrolatum | 7.65 | 7.65 | 7.65 |
| Carnauba | 1.30 | 1.30 | 1.30 |
| | | | |
| | 100.00 | 100.00 | 100.00 |

* no INCI name

0986541-03002

Table 3

| Component INCI | Comparison 4 | 4a | 4b |
|----------------------------|-----------------|--------|--------|
| Glyceryl stearate | 9.00 | 9.00 | 9.00 |
| Isopropyl myristate | 2.25 | 2.25 | 2.25 |
| Cetyl alcohol | 1.50 | 1.50 | 1.50 |
| Parabens | 0.35 | 0.35 | 0.35 |
| | | | |
| | | | |
| Demineralized water (aqua) | 62.27 | 62.27 | 62.27 |
| Allantoin | 0.25 | 0.25 | 0.25 |
| Xanthan gum | 0.30 | 0.30 | 0.30 |
| | | | |
| | | | |
| Propylene glycol | 8.90 | 8.90 | 8.90 |
| Iron oxide | 0.68 | 0.68 | 0.68 |
| Titanium dioxide * | 2.75 | 2.75 | 2.75 |
| | | | |
| | | | |
| Demineralized water (aqua) | 10.00 | 8.00 | 5.00 |
| Poly- α -glucan* | | 2.00 | 5.00 |
| | | | |
| | | | |
| Perfume (fragrance) | 0.25 | 0.25 | 0.25 |
| Demineralized water (aqua) | 1.00 | 1.00 | 1.00 |
| Imidazolidinylurea | 0.50 | 0.50 | 0.50 |
| | | | |
| | 100.00 | 100.00 | 100.00 |

* no INCI name

09869514-022000

Example 5

In-vitro production of poly-1,4- α -D-glucan in a biocatalytic process using amylosucrase.

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10 l of a 20% strength sucrose solution are added to a sterilized (steam sterilization) 15 l vessel. The enzyme extract, comprising amylosucrase, is added in one portion. The enzyme activity in this experiment is 16 units. The apparatus is provided with a likewise sterilized precision-ground glass paddle stirrer. The vessel is sealed and stirred at 37°C. After a period of just a few hours, a white precipitate forms. The reaction is complete after a period of 180 hours. The precipitate is filtered off and, to remove low molecular weight sugars washed five times with water. The residue which remains in the filter is dried at 40°C in a drying cabinet with application of a vacuum using a membrane pump (Vacuubrand GmbH & Co., CVC 2). The mass is 685 g (yield 69%).

15

Example 6

20 Characterization of the water-insoluble 1,4- α -D-linear poly-1,4- α -D-glucan from Example 1 synthesized using amylosucrase

2 mg of the poly-1,4- α -D-glucan from Example 1 are dissolved at room temperature in dimethyl sulfoxide (DMSO, p.a. from Riedel-de-Haen) and filtered (2 μ m filter). Some of the solution is injected into a gel permeation chromatography column. The mobile phase used is DMSO. The signal intensity is measured using an RI detector and evaluated against a pullulan standard (Polymer Standard Systems). The flow rate is 1.0 ml per minute.

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30 The measurement gives a number-average molecular weight (M_n) of 14,200 g/mol and a weight-average molecular weight (M_w) of 29,500 g/mol. This corresponds to a dispersity of 2.1.

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